

## REMARKS

### Objection to the Specification under 35 U.S.C. 112:

Claims 1 and 3-17 have been rejected under §112. Applicants have amended the claims to obviate the rejection. Examiner states that the as-filed specification only provides sufficient description of a chelator-polycationic polymer. For electrostatic interaction of a polychelator with a polynucleotide, the polychelator is in fact a polycation as the examiner states. However, a polychelator may be a polycation because of cations coordinated by the chelating groups, see example 2 on pages 18-19 of the specification. In the absence of the cation, the polychelator can be positively charged, negatively charged or charge neutral. Thus, for certain polychelators, interaction of the polynucleotide with the polychelator is ion concentration dependent, see example 5-6, on pages 21-23 of the specification. This same principle can be applied to a wide range of chelator electrostatic interactions as indicated in the specifications.

### Rejection of claims under 35 U.S.C. 102:

Claims 1, 3, 6-14 and 16-17 are rejected under §102(e) as being anticipated by Kayyem, WO 96/11712, IDS. Applicants have amended claim 1 to differentiate the claim from WO 96/11712.

Applicants believe that Kayyem relies on known nucleic acid delivery vehicles, such a polylysine-transferrin conjugates, which were described as early as 1990 (Zenke et al. PNAS 1990; and Wagner et al. PNAS 1990, enclosed). As such, Applicants believe that Kayyem solely teaches the co-delivery of an atom that is coordinately bound by a chelator together with nucleic acid. Furthermore, in the method taught by Kayyem, all targeting agents are attached to the polyamine or nucleic acid via a covalent linkage. The instant application teaches the use of chelators or polychelators to facilitate non-covalent, reversible interaction of components of a nucleic acid delivery system where coordination of a metal ion or amine facilitates or stabilizes the interaction. Applicants have amended claim 1 to specify that interaction of the chelator with components of a complex is dependent on coordination of a metal ion. Claim 1 now also incorporates previous claims 3 and 6. New independent claim 28 recites the interaction of a chelator with components of a polynucleotide delivery system through coordinate bonding of an amine. Claim 28 additionally incorporates previous claims 13 and 14. New independent claim 41 recites a polynucleotide delivery system that incorporates at least two molecules that each contain at least one covalently linked chelator. Interaction of these two molecules is stabilized by coordination of a metal ion by the chelator.

Several of the new claims are related to previous claims as follows:

- New claim 19 is predominantly old claim 4.
- New claim 20 is predominantly old claim 5.
- New claim 24 incorporates old claim 9.
- New dependent claim 21 incorporates old independent claim 10.
- New claims 22 and 23 incorporate old claim 11.
- New dependent claim 21 incorporates old independent claim 12.
- New claim 21 is predominantly old claim 15.

New claim 36 is predominantly old claim 17.

Rejection of claims under 35 U.S.C. 103:

The claims have been rejected under §103(a) as being unpatentable over Kayyem et al. taken with Hnatowich et al. (US Pat No 5,980,861).


It is the Applicants' opinion that Kayyem and Hnatowich teach the covalent attachment of a chelator to a known delivery vehicle for the purposes of co-delivery of a contrast agent atom (Kayyem) or a radionuclide atom (Hnatowich), and that both rely on methods known in the art for delivery of the nucleic acid to a cell. In contrast, Applicants teach the use of a chelator to facilitate reversible interaction of components of a polynucleotide delivery system, either through coordinate bonding of a metal ion or a primary amine. These distinctions are unique to Applicants' application and separate their processes from those of the prior art.

The examiners states that Hnatowich teaches non-covalent bonding of a chelator to a polymer (page 11 of the action). Applicants respectfully disagree. Hnatowich discusses non-covalent and ionic interaction only once, and then to refer to the coordinate binding of an atom by a chelator (column 10, line 66 through column 11, line1): "The term "chelator", as used herein, refers to a moiety that is capable of binding a radionuclide, preferably through non-covalent interactions, e.g., through ionic interactions."

The amendments and discussion from the previous sections apply to §103 as well. Applicants submit that the claims, as amended, are not obvious in view of the prior art.

The Examiner's objections and rejections are now believed to be overcome by this response to the Office Action. In view of Applicants' amendments and discussion, it is submitted that claims 1, 18-46 should be allowable and Applicants respectfully request an early notice to such effect.

Respectfully submitted,

  
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I hereby certify that this correspondence is being sent by facsimile transmission to: CM1 Fax Center at (703) 305-7401; Commissioner for Patents, Washington, DC 20231, on 4/14/03

  
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